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A Preliminary Toxicological Study of PYX Explosive

[2,6-bis(picrylamino)-3,5-dinitropyridine]

University of California

LOS ALAMOS SCIENTIFIC LABORATORY

Post Office Box 1663 Los Alamos, New Mexico 87545

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G. A. Drake
J. E. London
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A PRELIMINARY TOXICOLOGICAL STUDY OF PYX EXPLOSIVE [2,6-bis(picrylamino)-3,5-dinitropyridine]

by

G. A. Drake, J. E. London, and D. M. Smith

ABSTRACT

The acute oral LD_{30}^{50} values for PYX explosive for mice and rats is greater than 5 g/kg. According to classical guidelines, the material would be considered slightly or practically nontoxic in both species. Skin application studies in the rabbit with PYX explosive demonstrated that it was cutaneously nonirritating. This material was a very mild and transitory irritant in rabbit eye application studies. The sensitization study in the guinea pig did not show PYX explosive to be deleterious in this regard, although a firm thickening and erythema were seen at the injection sites 72 h after administration.

I. INTRODUCTION

As part of Los Alamos National Laboratory Toxicology Group's (LS-1) applied toxicology program, PYX explosive [2,6-bis(picrylamino)-3,5-dinitropyridine] was examined in the following tests: (1) acute oral toxicity; (2) primary skin irritation; (3) skin sensitization; and (4) conjunctival instillation. This thermally-stable explosive may have utility as a booster material for TATB-based compositions.

II. EXPERIMENTAL PROCEDURES

A. General

The PYX was supplied in 50 g samples by Group WX-2 of the Laboratory's Design Engineering Division. When not being used, the material was stored in the dark in a plastic container enclosed in a plastic bag in a locked safe file. A maximum dose of 5 g/kg was used for testing. If a material causes no mortality

at this level in 30 days it is reported as having an LD_{30}^{50} of greater than 5 g/kg and is considered to be slightly toxic or practically nontoxic.

B. Single-Dose Acute Oral Toxicity (LD_{30}^{50} Days)

1. Rats. Twenty young male adult (83-day-old) Sprague-Dawley rats (Charles River, Wilmington, MA), weighing 200 to 240 g, were used in the 5 g/kg test group to determine the range of toxicity.[1,2] The material was administered to ether-sedated, fasted rats by intragastric intubation as a suspension in corn oil using a ball-tipped 19-gauge needle and syringe. Corn oil was used to suspend the material because it is innocuous.

After treatment, all animals were observed daily for 30 days for aberrant physiological and behavioral responses. The data are on file with Los Alamos Group LS-1 as Compound LS-1-No. 15.

2. Mice. The procedure for single-dose oral-toxicity determination in mice was the same as for rats. Twenty young female adult (81-day-old) CFW-SW mice, (Charles River, Wilmington, MA) weighing 20 to 24 g were used. All animals were observed daily for 30 days after treatment.

C. Primary Skin Irritation

The Draize test[3] was used to assess primary skin irritation. Six New Zealand white rabbits (Keen Ridge Rabbit Ranch, Edgewood, New Mexico) weighing 3.0 to 4.5 kg each, were used. The back of each rabbit was clipped free of hair 24 hr before application of the mixture using Oster electric clippers (Oster Corporation, Racine, Wisconsin) with a No. 40 blade. Four sites, two intact and two abraded, were established. The material was applied as a paste (500 mg in 0.5 mℓ of corn oil) at each location. The test sites were covered with a gauze pad, and the entire back was overlaid with an adhesive plastic surgical drape. Each rabbit was then placed in a rabbit jacket (Alice King Chatham, Los Angeles, California). The jackets and wraps were removed 24 h later, and each test site was scored visually for erythema and edema. Readings were recorded at 24, 48, and 72 h. A final irritation score was calculated for the 24- and 72-h readings.

D. Ocular Irritation

Six New Zealand white rabbits (Keen Ridge Rabbit Ranch, Edgewood, New Mexico) weighing 2.0 to 3.1 kg each, were used in this test. Both eyes were checked for abnormalities before instillation. The material (100 mg) was instilled into the conjunctival envelope of the left eye of each rabbit; the right eye served as a control. Two rabbits had the material washed from the eye with 0.15 M NaCl at 30 s after instillation, two at 5 min after instillation, and two

did not have the material washed from the eye. Each eye was graded for ocular lesions at 1, 4, 24, 48, and 72 h. Of particular interest was whether the cornea, iris, and conjunctivae became inflamed. The procedure and grading systems were taken from the Draize test.[3]

E. Skin Sensitization

Eight female English guinea pigs (Camm Research Institute, Wayne, New Jersey) weighing 581 to 781 g, were used. The animals were housed individually and fed commercial laboratory stock diets ad libitum supplemented daily by lettuce and cabbage. One hundred mg of the PYX explosive was diluted to 100 mℓ with corn oil to make a 0.1% solution for injection. Corn oil controls were previously tested and found to be innocuous.[4] The material was administered in a series of 10 "sensitizing" injections into the lower back and flanks of the guinea pigs. Before each injection, the test sites were clipped free of hair. Intradermal injections were made randomly over the test area on Sunday, Tuesday, and Thursday with a 1-mℓ tuberculin syringe fitted with a 25-gauge needle. The volume of the first injection was 0.05 mℓ, and the remaining nine were each 0.1 mℓ. At 24 h after each injection, the sites were scored for erythema (redness), height, and diameter. Redness and height were scored as described by Landsteiner and Jacobs.[5] The diameters of the reactions were measured in millimeters using a micrometer caliper. At 2 wk after administration of the tenth sensitizing injection, the lower back and flanks of each guinea pig were clipped free of hair, and a challenge injection of 0.05 mℓ was administered. The reaction of each animal was graded 24 h later and compared with results from the sensitizing injections.

III. RESULTS AND DISCUSSION

A. Single-Dose Acute Oral Toxicity (LD_{30}^{50} Days)

1. Rats. In general, all rat behavioral and physiological responses after administration appeared normal for 30 days. The LD_{30}^{50} value was greater than 5 g/kg.

2. Mice. All mouse behavioral and physiological responses after administration appeared normal. The LD_{30}^{50} value was greater than 5 g/kg.

B. Primary Skin Irritation

The PYX explosive caused no edema or erythema on the abraded and unabraded treated rabbits; therefore, the primary skin irritation studies demonstrated that the compound was nonirritating. The total primary irritation score was 0.00.

C. Eye Irritation

Table I summarizes the eye irritation responses of PYX explosive. Irritation was observed only in conjunctival tissue. Conjunctival responses were observed at all treatment levels at 1 h and generally consisted of mild redness and mucoid exudation. All treatment groups were judged normal in 24 h. The eye irritation caused by PYX explosive was very mild and transitory.

D. Skin Sensitization

Review of the data collected for each guinea pig in the treatment group indicates that all challenge injection reactions were within the limits of the reactions recorded during the sensitizing period. The guinea pig skin sensitization study did not show PYX explosive to be a sensitizer. However, in some animals (7 of 8), areas of firm thickening and erythemia developed at each injection site 72 h after intradermal administration of this material.

TABLE I

EYE IRRITATION RESPONSE IN RABBITS TREATED WITH PYX EXPLOSIVE[a]

	Average Irritation[b] (hours)		(days)		
Tissue Graded	1	4	1	2	3
Wash at 30 s					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	2	3	0	0	0
Wash at 5 min					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	1	2	0	0	0
No Wash					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	3	3	0	0	0

[a] Two rabbits per wash condition.

[b] Maximum cornea response = 80; maximum iris response = 10; maximum conjunctivae response = 20.

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